Attorney Docket No. 54269.8002.US01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Group Art Unit: Thai-An N. Ton
Kangsheng Wang	)	Examiner: 1632
Serial No. 09/781,046	)	
Filed: February 8, 2001	)	
For: A Method and System for Introducing a Gene into a Human Stem Cell	)	

AFFIDAVIT OF KIRON KANGSHENG WANG

PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Madam:

I, Kangsheng Wang, hereby declare, subject to penalty of perjury, as follows:.

1. I am currently President and Chief Executive Officer of BioAgri Corporation ; I have been involved in the research of molecular biology for over 22 years; I obtained a Ph.D. degree in Biology from the California Institute of Technology in 1991; I worked at Chiron Corporation as Research Associate for 3 years and Scientist for 7 years; and I have published about 12 research papers in well known scientific journals.

2. I have reviewed the United States Patent Application No. 09/781,046 entitled "A Method and System for Introducing A Gene Into A Human Stem Cell" filed February 8, 2001

(the '046 Application) and the United States Patent Application No. 09/573,861 entitled "A New Vector For Genetically Modifying Non-Human Animals" filed March 28, 2000 (the `861 Application), wherein the `046 Application is a continuation-in-part application of the `861 Application.

3. I am the sole inventor of the '046 and '861 Applications.

4. I have read and understood the Office Action dated April 26, 2002 and the Final Office Action dated February 11, 2003, regarding the `046 Application. The Final Office Action maintains the rejections of claims 22 – 26 of the `046 Application under 35 U.S.C.112, first paragraph, since the Final Office Action asserts that "in general antibodies directed to sperm would be expected to inhibit fertilization" and "it would have required undue experimentation for one skilled in the art to expect that the sperm-specific antibodies of the instant invention would retain the ability to fertilize an oocyte."

5. I have made more than one antibodies that bind to a sperm, retain the ability of the sperm bound with the antibody to fertilize an oocyte, and carry DNA into the oocyte from which a transgenic animal developed, through the use of the same method as disclosed in the `046 and `861 Applications.

6. I include a copy of pertinent pages of my original laboratory records dated from March 15, 1999 to February 8, 2001, as shown in Appendix A submitted herein.

Page 4 of the Appendix A demonstrates that mouse sperm cells were collected and used to immunize mice to produce antibodies against the sperm cells. This procedure is identical to what was described in Example I of the `861 Application (p. 10, ll. 20-21, the `861 Application).

Pages 6 to 10 of the Appendix A show that a number of hybridoma supernatants generated from the mice immunized by mice sperm cells do not prohibit sperms from fertilizing oocytes. In particular, hybridoma supernatants were incubated with sperm cells first and the mixture was incubated with oocytes for *in vitro* fertilization (Page 6). It was observed that hybridoma supernatants nos. 1B3, 1F5, 2D4, 2E8, 3C7, 4E7 did not inhibit fertilization. In a re-testing process, sub-supernatant 1A8 from 1B3, sub-supernatant 1F3 from 2D4, sub-supernatant 2C5 from 3C7, sub-supernatant 2G5 from 2E8, sub-supernatant 1F11 from 4E7, and sub-supernatant 1D8 from 1F5 all retained fertilization (Page 9 of the Appendix A).

Pages 12 to 20 of the Appendix A illustrate that the hybridoma supernatants that retained fertilization contained antibodies that bind to sperm cells. As shown in page 10, hybridoma supernatants 1B3(1A8), 2D4 (1F3), 3C7(2C5), 2E8(2G5), 4E7(1F11), 1F5(1D8) were marked as mouse antibody A, B, C, D, E and F respectively. The flow cytometry method as disclosed in Example I of the `861 Application (p. 10, l. 21 to p. 11, ll. 8, the `861 Application) was conducted to determine whether the antibodies bind to sperm cells. It was observed that mouse antibody A (mAbA) bound to mouse sperm cells (Page 17), so did mAbB (Page 18), mAbC (Page 19), and mAbD (Page 20).

Pages 22 to 23 further illustrate that mAbC and mAbD both have shown to carry transgene DNA into an oocyte from which a transgenic mouse develops. The procedures to generate a transgenic mouse are identical to Example IV of the `861 Application (p. 15, l. 1 to p. 16, l. 6 of the `861 Application). The Southern blot analysis was performed to confirm whether the transgene DNA was integrated into the genome of the transgenic mouse (Example IV of the `861 Application). As shown in page 22 of the Appendix A, the transgenic mice generated using

mAbC contained the transgene in their genome. The transgenic mice generated using mAbD also contained the transgene their genome (page 23 of the Appendix A).

In light of the foregoing, it is concluded that a number of antibodies, including 1B3(1A8), 2D4 (1F3), 3C7(2C5), 2E8(2G5), 4E7(1F11), and 1F5(1D8), have been made according to the method disclosed in the '861 Application, and have binding affinity to sperm cells and the sperm cells bound with the antibodies retain the ability to fertilize oocytes. In addition, more than one antibody (mAbC and mAbD) has demonstrated that sperm cells bound with the antibody are able to carry transgene DNA and fertilize an oocyte from which a transgenic animal develops and contains the transgene.

7. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and, further, that these statements are made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of United States Applications No. 09/781,046 and United States Patent Application No. 09/573,861, any patent issuing thereon, or any patent to which this verified statement is directed.

Executed and signed on July 10, 2003, at City of Industry, California.

Kangsheng Wang